US009163002B2

(12) **United States Patent**
Wang et al.

(10) **Patent No.:** **US 9,163,002 B2**
(45) **Date of Patent:** **Oct. 20, 2015**

(54) **METHODOLOGY FOR THE SYNTHESIS OF XANTHONES**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/049,809**

(22) Filed: **Oct. 9, 2013**

(65) **Prior Publication Data**

US 2014/0107354 A1 Apr. 17, 2014

Related U.S. Application Data

(60) Provisional application No. 61/795,215, filed on Oct. 12, 2012.

(51) **Int. Cl.**
C07D 311/86 (2006.01)

(52) **U.S. Cl.**
CPC ***C07D 311/86*** (2013.01)

(58) **Field of Classification Search**
CPC C07D 311/86
See application file for complete search history.

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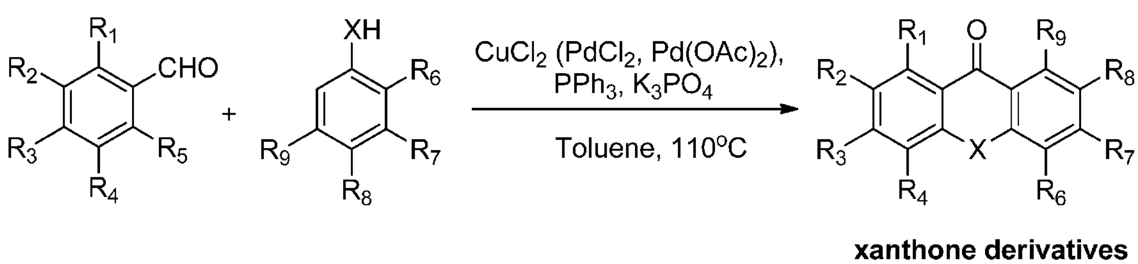
(57) **ABSTRACT**

Methods are provided for forming a xanthone derivative via reacting a 2-substituted benzaldehyde with a phenol derivative to form the xanthone derivative.

13 Claims, 11 Drawing Sheets



R_1, R_2, R_3, R_4, R_6, R_7, R_8, R_9 = aryl, alkyl, alkoxy, halide, amine, hydroxyl, nitro, cyano

R_5= F, Cl, Br, I, nitro, alkoxy

X=O, S, NH

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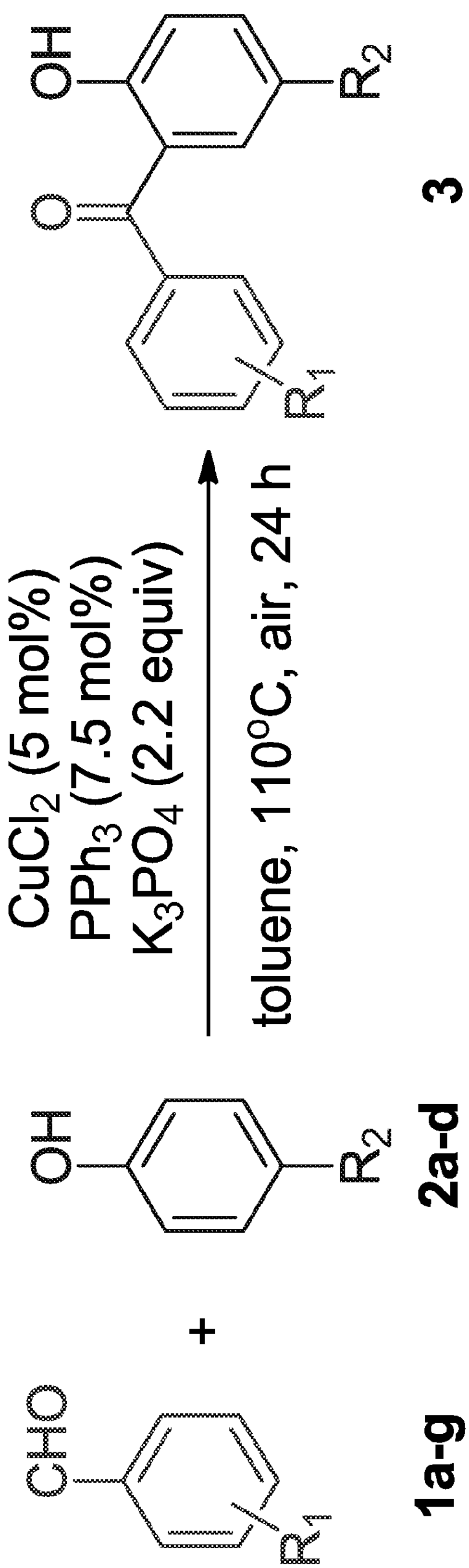

CHO
R1
1a-g
+
OH
R2
2a-d
CuCl2 (5 mol%)
PPh3 (7.5 mol%)
K3PO4 (2.2 equiv)
toluene, 110°C, air, 24 h
O
OH
R1
R2
3

Fig. 1

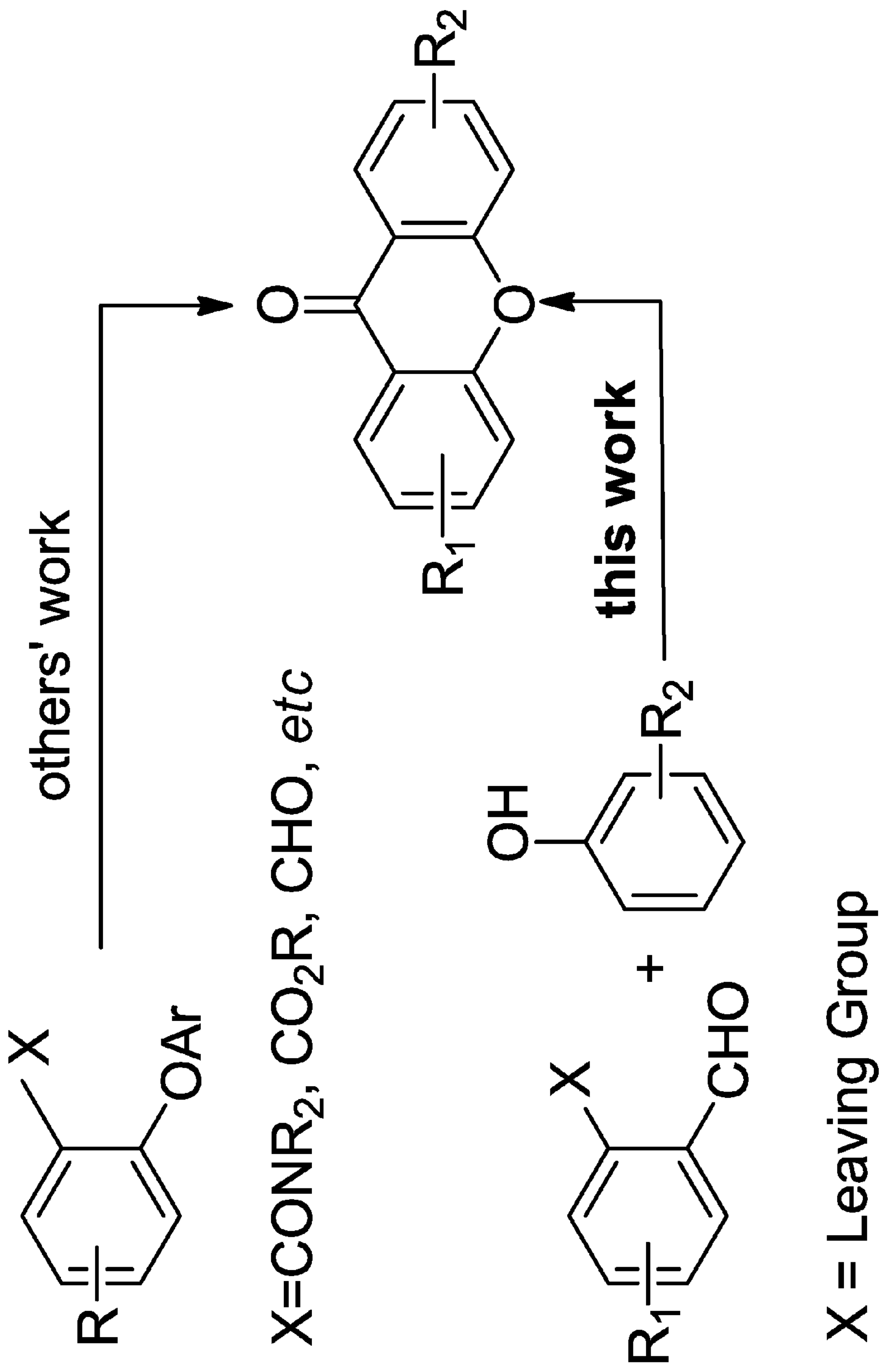

others' work
this work
OAr
X
R
$X=CONR_2$, CO_2R, CHO, *etc*
CHO
OH
R_1
R_2
+
X = Leaving Group
O

Fig. 2

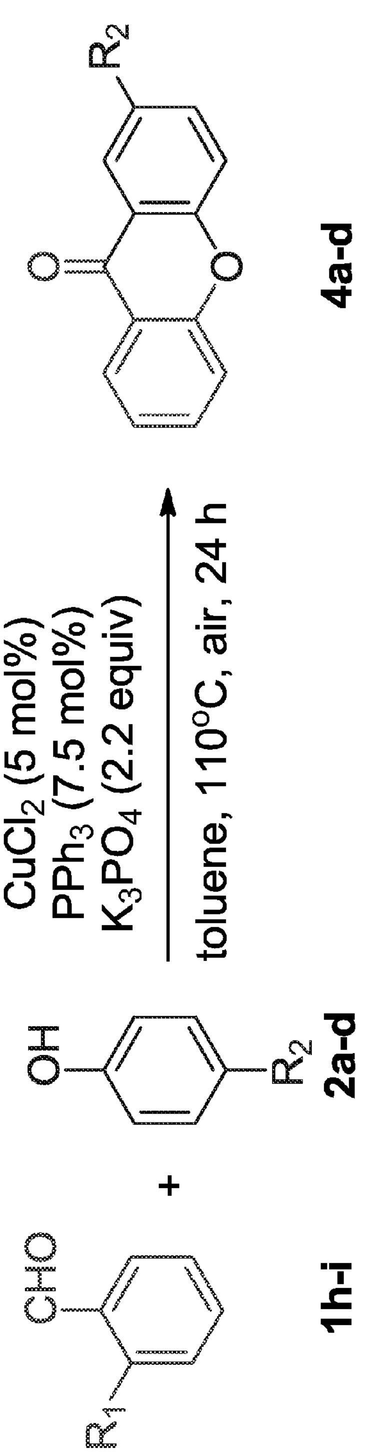

CHO
R_1
1h-i
+
OH
R_2
2a-d
$CuCl_2$ (5 mol%)
PPh_3 (7.5 mol%)
K_3PO_4 (2.2 equiv)
toluene, 110°C, air, 24 h
O
O
R_2
4a-d

Fig. 3

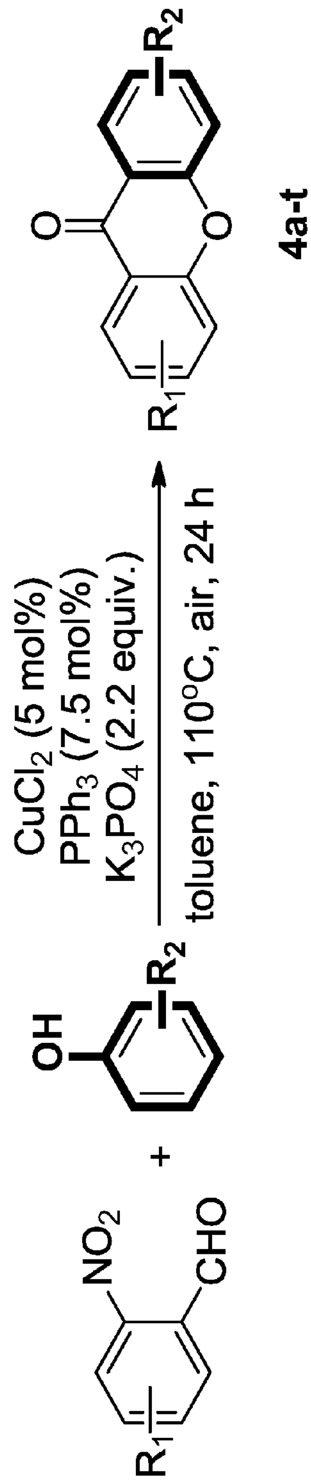
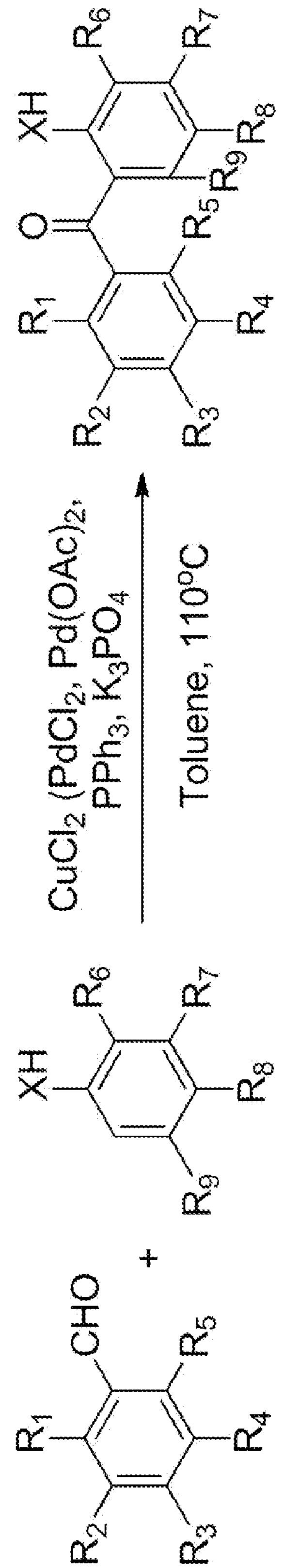

NO_2
CHO
R_1
+
OH
R_2
$CuCl_2$ (5 mol%)
PPh_3 (7.5 mol%)
K_3PO_4 (2.2 equiv.)
toluene, 110°C, air, 24 h
O
O
R_1
R_2
4a-t

Fig. 4



$R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9$ = aryl, alkyl, alkoxy, halide, amine, hydroxyl, nitro, cyano

X=O, NH,S

Fig. 5

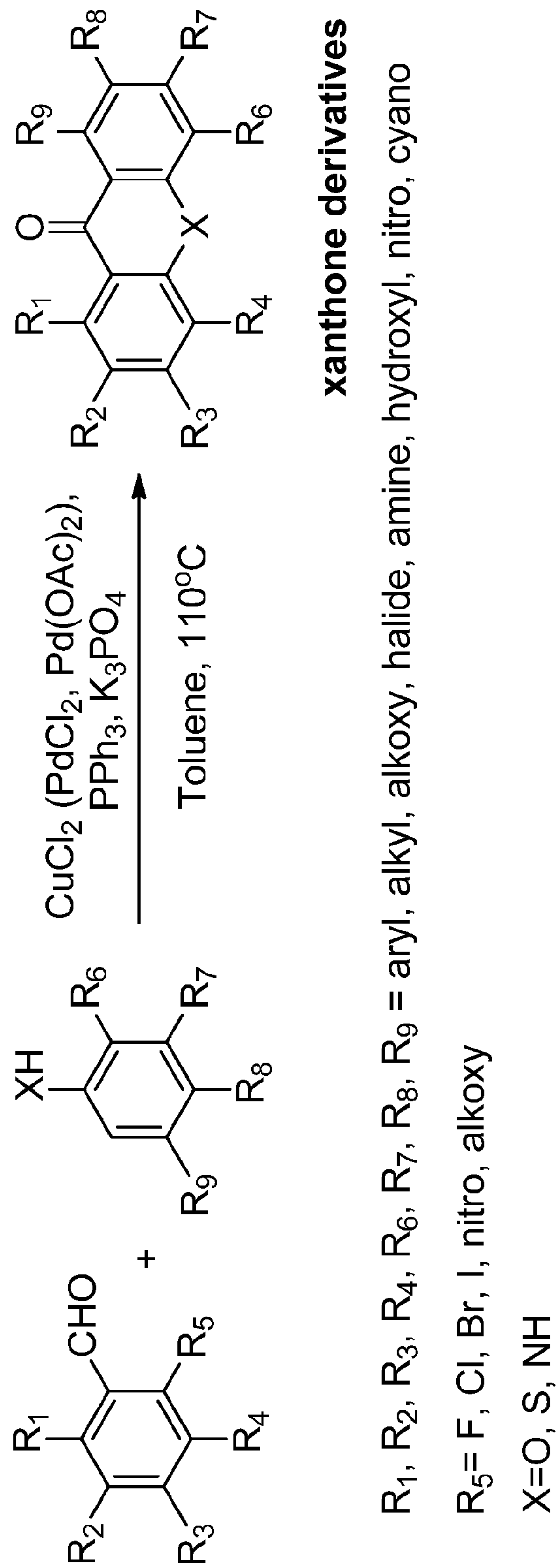

CuCl2 (PdCl2, Pd(OAc)2),
PPh3, K3PO4
Toluene, 110°C
xanthone derivatives
R1, R2, R3, R4, R6, R7, R8, R9 = aryl, alkyl, alkoxy, halide, amine, hydroxyl, nitro, cyano
R5= F, Cl, Br, I, nitro, alkoxy
X=O, S, NH

Fig. 6

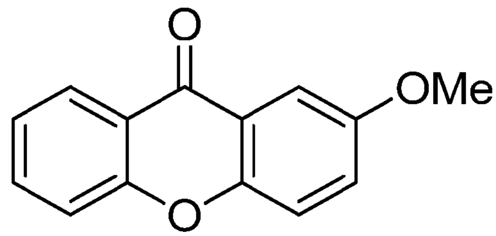


Fig. 7A

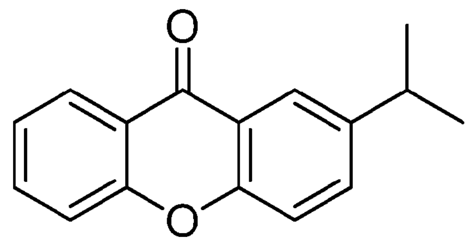


Fig. 7B

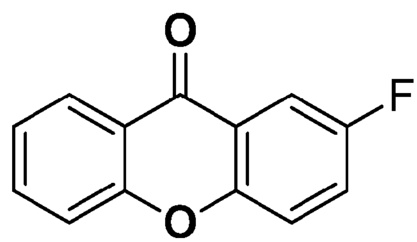


Fig. 7C

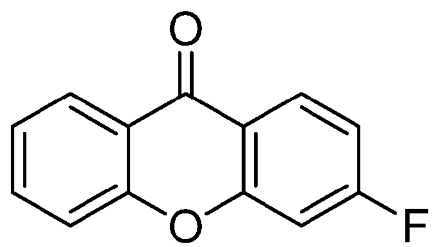


Fig. 7D

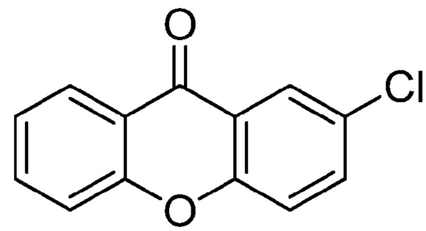


Fig. 7E

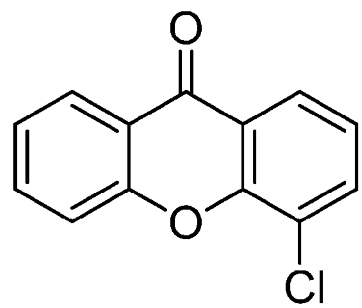


Fig. 7F

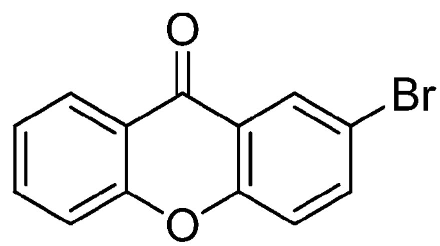
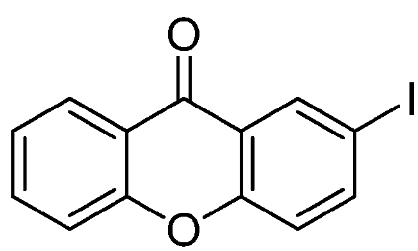


Fig. 7G



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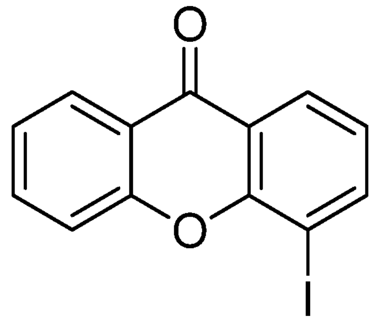


Fig. 7I

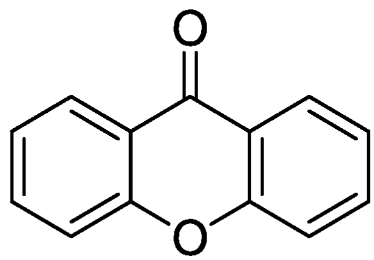
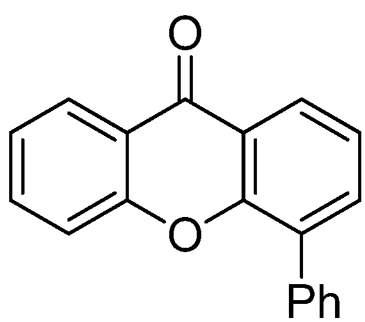


Fig. 7J



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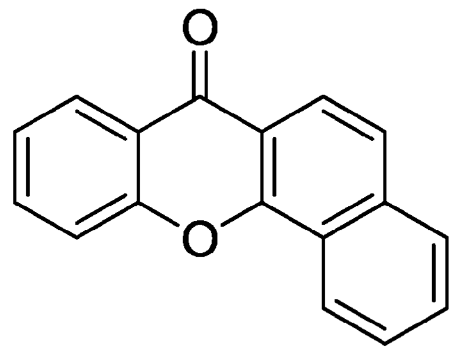

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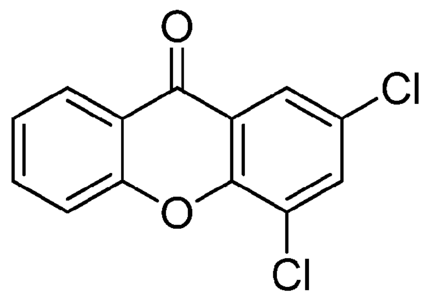
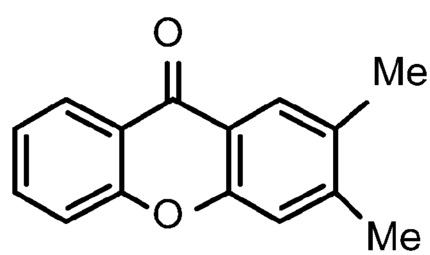


Fig. 7M



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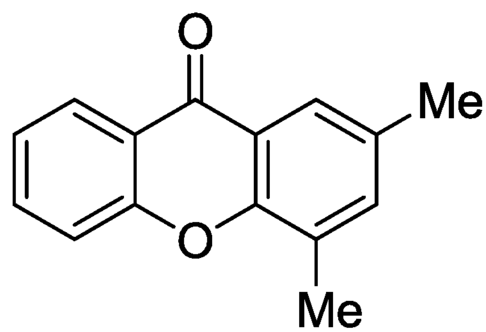
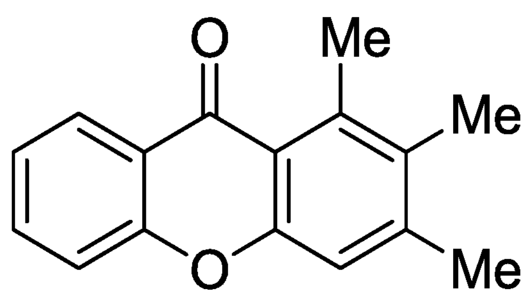


Fig. 7O



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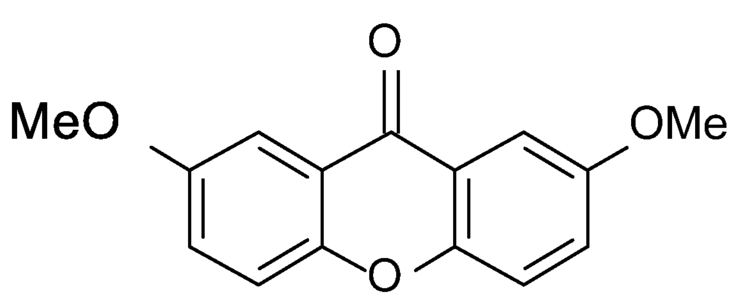

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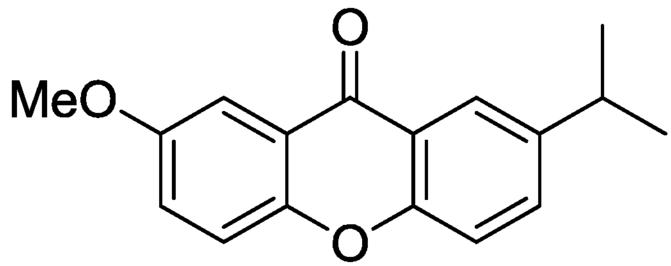


Fig. 7R

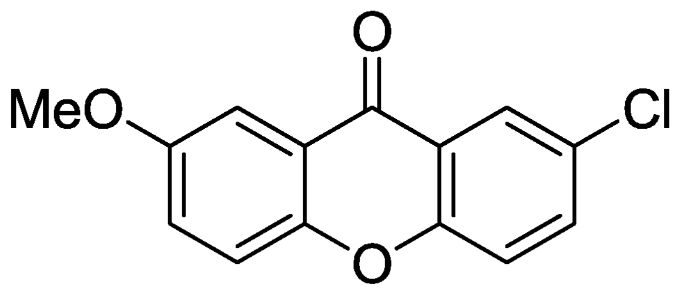


Fig. 7S

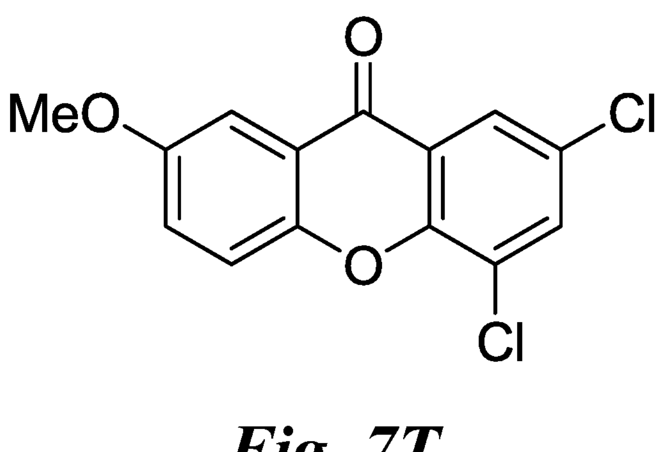


Fig. 7T

METHODOLOGY FOR THE SYNTHESIS OF XANTHONES

PRIORITY INFORMATION

The present application claims priority to U.S. Provisional Patent Application Ser. No. 61/795,215 of Wang, et al. filed on Oct. 12, 2012, the disclosure of which is incorporated by reference herein.

BACKGROUND

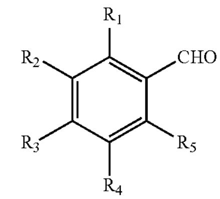
Direct acylation of phenolic C—H bond usually attracts much attention since phenols are one of the most important aromatic compounds in nature and industry. Two major categories of pathways can be followed in this transformation, namely, the most well-known powerful Lewis acid-catalyzed Friedel-Crafts acylation pathway, and the transition-metal-catalyzed C—H activation pathway. However, Friedel-Crafts acylation reaction is usually difficult to control the regio- and/or mono-selectivity if no directing group is present in the benzene ring, and it often suffers from the harsh reaction condition, usage of air/water sensitive Lewis acid and incompatibility with many functional groups. Meanwhile, although transition-metal-catalyzed C—H activation can direct converting carbon-hydrogen bond into carbon-oxygen, carbon-nitrogen, carbon-halide, carbon-sulfur, or carbon-carbon bonds, till now, there is no report about C—H activation in acylation reaction of unprotected phenols. To our knowledge, only one work has been published reporting the acylation of 1-naphthol with benzaldehyde catalyzed by $Pd(OAc)_2$ in the presence of triphenylphosphine. In that paper, Miura and coworkers didn't carry out an in-depth investigation of the reaction scope, and the reaction conditions were not optimized, while they just used this reaction as a control when they synthesized benzofuran-2(3H)-ones.

Xanthones are important structural units in organic chemistry and widely presented in natural products, and their derivatives were reported to show diverse physicochemical and pharmacological properties such as antioxidants, antiinflammatory, antineoplastic, and vasodilator. Albeit many methods are available for their syntheses, most of them either require advanced starting materials, involve multistep transformations, or exotic reaction conditions, more frequently, via the Friedel-Crafts reactions. There were only a few one-step synthesis of xanthones existed in literature. For example, Larock et al. reported the one-pot synthesis of xanthones by the tandem coupling-cyclization of arynes and salicylates. The same group also reported a C—H activation approach where an arylated imidoyl palladium intermediate promoted the intramolecular arylation resulted in xanthone skeletons. Another elegant work from Li group showed that 2-aryloxybenzaldehyde can undergo an intramolecular cross-dehydrogenative coupling reaction to form xanthones smoothly.

SUMMARY

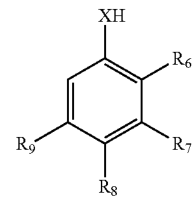
Objects and advantages of the invention will be set forth in part in the following description, or may be obvious from the description, or may be learned through practice of the invention.

Methods are generally provided for forming a xanthone derivative via reacting a 2-substituted benzaldehyde with a phenol derivative to form the xanthone derivative. In one embodiment, the 2-substituted benzaldehyde has a structure:



where R_1, R_2, R_3, and R_4 are, independently, H, an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group; and where R_5 is F, Cl, Br, I, a nitro group, or an alkoxy group.

The phenol derivative, in one particular embodiment, has a structure:



where R_6, R_7, R_8, and R_9 are, independently, H, an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group; and X is O, S, or NH.

Other features and aspects of the present invention are discussed in greater detail below.

BRIEF DESCRIPTION OF THE DRAWINGS

A full and enabling disclosure of the present invention, including the best mode thereof to one skilled in the art, is set forth more particularly in the remainder of the specification, which includes reference to the accompanying figures, in which:

FIG. **1** shows a general schematic of a reaction for ortho-acylation of phenols with aryl aldehydes;

FIG. **2** shows a general schematic of different reaction methods for one step synthesis of xanthone derivatives;

FIG. **3** shows a general schematic of an exemplary reaction method for one step synthesis of a xanthone derivative;

FIG. **4** shows a general schematic of an exemplary reaction method for one step synthesis of a xanthone derivative;

FIG. **5** shows a general schematic of an exemplary intermolecular ortho-acylation reaction of phenols with aryl aldehydes;

FIG. **6** shows a general schematic of an exemplary reaction method for one step synthesis of a xanthone derivative; and

FIGS. **7A-7T** show exemplary xanthone derivatives formed according to the Examples.

Repeat use of reference characters in the present specification and drawings is intended to represent the same or analogous features or elements of the present invention.

DETAILED DESCRIPTION

Reference now will be made to the embodiments of the invention, one or more examples of which are set forth below. Each example is provided by way of an explanation of the invention, not as a limitation of the invention. In fact, it will be apparent to those skilled in the art that various modifications and variations can be made in the invention without departing from the scope or spirit of the invention. For instance, features illustrated or described as one embodiment can be used on another embodiment to yield still a further embodiment. Thus, it is intended that the present invention cover such modifications and variations as come within the scope of the appended claims and their equivalents. It is to be understood by one of ordinary skill in the art that the present discussion is a description of exemplary embodiments only, and is not intended as limiting the broader aspects of the present invention, which broader aspects are embodied exemplary constructions.

Generally speaking, the present disclosure is directed to a novel ortho-acylation reaction which can be realized with excellent yields under mild conditions. This method can be used to synthesize the xanthone derivatives. As used herein, the term "xanthone derivative" includes any molecule that has the base structure of xanthone, with or without substitutions. As such, the term "xanthone derivative" may include xanthone unless otherwise specified.

I. Acylation of Phenols with Aryl Aldehydes

In the presence of triphenylphosphine, copper (II) chloride can catalyze an intermolecular ortho-acylation reaction of phenols with aryl aldehydes. To investigate the optimized reaction protocol, a systematic screening of catalysts, ligands, and bases was carried out. Finally, we chose 1 mmol aldehyde, 1.3 mmol phenol in toluene at 110° C. in the presence of 5 mol % of $CuCl_2$, 7.5 mol % PPh_3 and K_3PO_4 (2.2 equiv.) as the standard reaction condition. However, similar reactions can also be applied.

FIG. **1** and Table 1 show, collectively, a few examples demonstrating the reaction scope of this reaction with various phenols and aryl aldehydes. The results showed that regardless of the substitution of aryl aldehydes, electron withdrawing or donating, all compounds furnished the desired ortho-acylation products in almost similar yields when reacted with the same phenol (70%-91% entries 1-7; 63%-94% entries 8-12; 42%-78% entries 13-16); even the 4-nitrobenzaldehyde produced a 70% yield (entry 12). The stronger electron-donating group phenols possessed, the more effective the acylation reactions were.

TABLE 1

Ortho-acylation of phenols with aryl aldehydes (see FIG. 1)

entry		R_1		R_2	product	Yield (%)
1	1a	3-OCH_3	2a	OCH_3	3aa	91[b] (79)[c]
2	1b	4-CH_3	2a	OCH_3	3ba	70 (60)
3	1c	H	2a	OCH_3	3ca	79 (64)
4	1d	3-Cl	2a	OCH_3	3da	83 (70)
5	1e	4-F	2a	OCH_3	3ea	84 (73)
7	1f	2,6-OCH_3	2a	OCH_3	3fa	77 (65)
8	1a	3-OCH_3	2b	i-Pr	3ab	94 (82)
9	1b	4-CH_3	2b	i-Pr	3bb	73 (60)
10	1c	H	2b	i-Pr	3cb	63 (48)
11	1d	3-Cl	2b	i-Pr	3db	92 (79)
12	1g	4-NO_2	2b	i-Pr	3gb	70 (58)
13	1a	3-OCH_3	2c	H	3ac	56 (47)
14	1b	4-CH_3	2c	H	3bc	64 (50)
15	1d	3-Cl	2c	H	3dc	78 (67)
16	1g	4-NO_2	2c	H	3gc	42 (31)
17[d]	1g	4-NO_2	2d	I	3gd	62 (51)
18	1a	3-OCH_3	2e	NO_2	—	—

[a]1 mmol aldehyde and 1.3 mmol phenol;
[b]^{1}H NMR yield;
[c]Isolated yield;
[d]Cross-coupling reaction between iodine and hydroxyl was observed besides the ortho-acylation reaction.

II. One Step Synthesis of Xanthone Derivatives

It was found that when 2-substituted aryl aldehyde (1h-j) reacted with phenols, xanthones were obtained with high-yield in one step (see, FIG. **3** and Table 2, collectively). Albeit many methods are available for the synthesis of xanthones, most of them either require advanced starting materials, exotic reaction conditions, or involve multistep transformations. There are only a few one-step synthesis of xanthones existing in literature. Hence, the presently disclosed method offers a concise and straightforward strategy to construct xanthones directly without the preactivation of aldehydes (see FIG. **2**).

A. Exemplary Reactions

As shown in FIG. **3** and Table 2, 2-methoxybenzaldehyde (1h) and 2-nitrobenzaldehyde (1i) produced the corresponding xanthones in excellent yields (entries 1, 2, 4, 6 and 8), while with 2-bromobenzaldehyde (1j) as the starting material, lower yields were observed, likely due to the cross-coupling reaction between bromo and hydroxyl groups (entries 3, 5 and 7, yields are listed in the footnote). It is believed that the ring-closed xanthone products are achieved via the ortho-acylation of phenols with 2-substituted aryl aldehydes first, and then under a basic condition, the ortho-substituents of aldehydes serving as leaving groups lead to the final ring-closed xanthones.

TABLE 2

One-step ortho-acylation of phenols with 2-substituted benzaldehydes to afford xanthones[a] (see FIG. 3)

entry		R_1		R_2	product	Yield %
1	1h	OCH_3	2a	OCH_3	4a	85[b] (71)[c]
2	1i	NO_2	2a	OCH_3	4a	87 (74)
3[d]	1j	Br	2a	OCH_3	4a	68 (52)
4	1i	NO_2	2b	i-Pr	4b	92 (81)
5[d]	1j	Br	2b	i-Pr	4b	64 (56)
6	1i	NO_2	2c	H	4c	81 (70)
7[d]	1j	Br	2c	H	4c	55 (43)
8	1i	NO_2	2d	I	4d	73 (62)

[a]1 mmol 2-substitued aldehydes and 1.3 mmol phenol;
[b]^{1}H NMR yield;
[c]Isolated yield;
[d]Cross-coupling reaction between bromo and hydroxyl was observed in entries 3 (17%), 5 (14%) and 7 (13%) besides the ortho-acylation reaction.

Since nitro group gave better results than other leaving groups, the reaction substrates of 2-nitrobenzaldehydes and phenols were investigated (FIG. **4** and Table 3, collectively). It showed that alkoxy, alkyl, aryl and halide substituents were tolerated on the phenols to furnish the desired xanthones affording moderate to excellent yields. While electron-donating groups on phenols can promote the reaction, electron-withdrawing groups (NO_2 or CN) will block the reaction completely (data not shown). If the substituted group was at the para position of the phenol, the yield was higher than it was at ortho position, possibly due to the steric effect (4d vs 4e, 4g vs 4h). The steric effect can also explain the excellent regioselectivity of this reaction (e.g. 4i was the sole product) as was as the sluggish reactivity of ortho-t-butylphenol (no product was observed). Disubstituted and trisubstituted xanthones could also be prepared via this copper-catalyzed ortho-acylation reaction affording moderate yields (4m-p and 4t).

TABLE 3

Scope of reaction of 2-nitrobenzaldehydes with phenols to prepare xanthones[a]

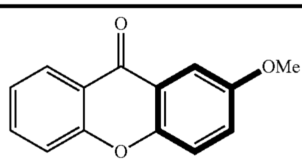
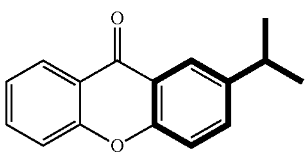
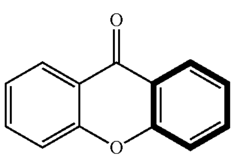
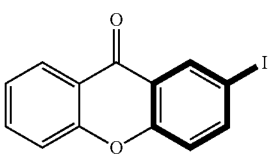
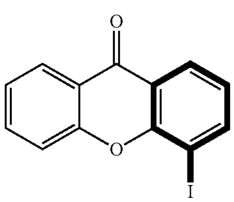
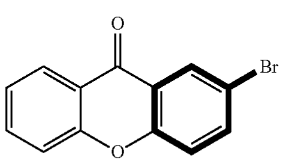
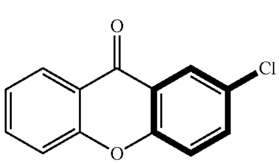
	Product	Yield (%)
4a		87[b](74)[c]
4b		92(81)
4c		81(70)
4d		77(62)
4e		73(62)
4f		72(59)
4g		82(73)

TABLE 3-continued

Scope of reaction of 2-nitrobenzaldehydes with phenols to prepare xanthones[a]

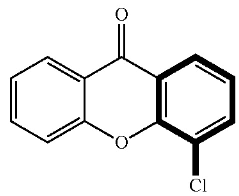
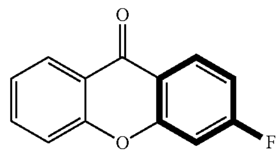
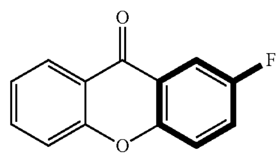
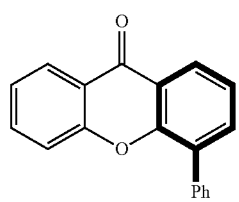
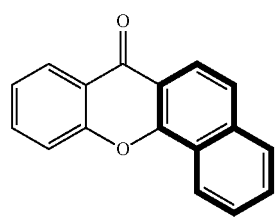
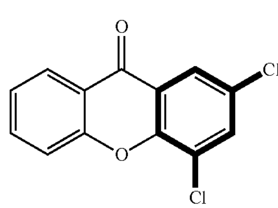
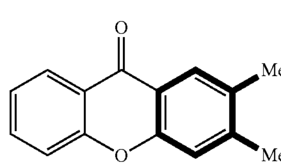
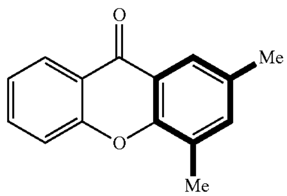
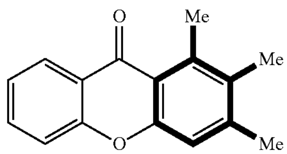
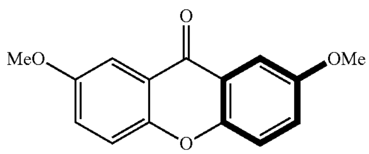
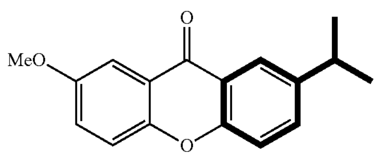
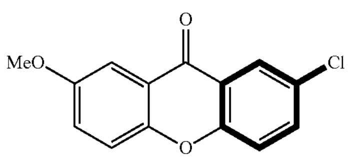
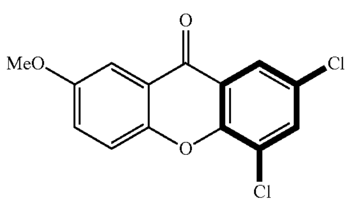
4h		76(60)
4i		70(58)
4j		71(55)
	Product	Yield[b] (%)
4k		69(55)
4l		43(30)
4m		75(64)
4n		84(72)

TABLE 3-continued

Scope of reaction of 2-nitrobenzaldehydes with phenols to prepare xanthones[a]		
4o		90(80)
4p		73(61)
4q		83(70)
4r		82(70)
4s		80(69)
4t		68(57)

[a]1 mmol 2-nitrobenzaldehydes, 1.3 mmol phenols;
[b]^{1}H NMR yield;
[c]Isolated yield.

B. Extension of Reaction Methods to Other Synthesis

As show in FIG. **5**, through the optimization of the reaction condition, we chose the system of 5 mol % of $CuCl_2$, $PdCl_2$, or $Pd(OAc)_2$, 7.5 mol % PPh_3, K_3PO_4 (2.2 equiv.) and the substrates in toluene at 110° C. as our standard reaction condition. However, this condition can be adjusted based on the structural diversity of different substrates. Using this system, a series of ortho-acylation derivatives of phenols and xanthone derivatives have been synthesized with high yields (FIGS. **5** and **6**).

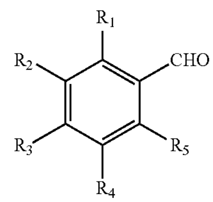
In conclusion, we have demonstrated the catalytic intermolecular ortho-acylation of phenols with various aryl aldehydes using copper/palladium as the catalyst in presence of the triphenyl-phosphine ligand, and it can be used to synthesize xanthone derivatives in one step with high yields.

Our reaction condition is considerably mild, and it offers an alternative to the widely used Lewis acid-catalyzed Friedel-Crafts acylation reaction that often suffers from the harsh reaction condition, usage of air/water sensitive Lewis acid and incompatibility with many functional groups.

C. 2-Substituted Benzaldehydes

In view of the above discussion, particularly suitable 2-substituted benzaldehydes have a structure of Formula I below:

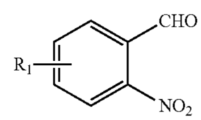
Formula I



where R_1, R_2, R_3, and R_4 are, independently, H, an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group; and where R_5 is F, Cl, Br, I, a nitro group, or an alkoxy group.

In particular embodiments, R_5 is a nitro group, and/or at least three of R_1, R_2, R_3, and R_4 are H (i.e., leaving only a single organic group extending from the ring). Such a benzaldehyde compound is shown in Formula II:

Formula II

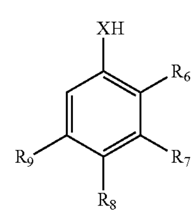


where R_1 is H, an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group.

D. Phenol Derivatives

Particularly suitable phenol derivatives have a structure of Formula III below:

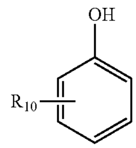
Formula III



where R_6, R_7, R_8, and R_9 are, independently, H, an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group; and X is O, S, or NH.

In particular embodiments, X is O, and/or at least three of R_6, R_7, R_8, and R_9 are H (i.e., leaving only a single organic group extending from the ring). Such a compound is shown in Formula IV:

Formula IV



where R_{10} is H, an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group.

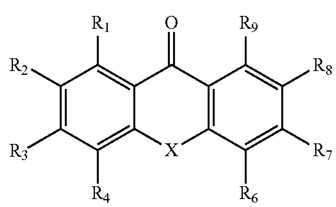
E. Reaction Conditions

The molar ratio of aldehydes to phenols can be about 1:1 to about 1:5, such as about 1.25 to about 1.35 (e.g., about 1:1.3). Generally, the triphenylphosphine is used as a ligand to the catalyst. In certain embodiments, the 2-substituted benzaldehyde is reacted with the phenol derivative in the presence of a catalyst system including a palladium catalyst (e.g., $PdCl_2$, $Pd(OAc)_2$, etc.) and a copper catalyst (e.g., $CuCl_2$). The ratio of these catalysts to the phenol can be about 2 mol % to about 10 mol % (e.g., about 5 mol %) Generally, the K_3PO_4 is used as the base for deportonation. All these experiments were carried out in an inert atmosphere (e.g., under the protection of nitrogen).

F. Xanthone Derivatives

Generally, the reaction of the 2-substituted benzaldehyde of Formula I with the phenol derivative of Formula III results in the formation of a xanthone derivative having the structure of Formula V:

Formula V



where R_1, R_2, R_3, R_4, R_6, R_7, R_8, and R_9 remain unchanged from their parent compounds described above (i.e., the 2-substituted benzaldehyde of Formula I and the phenol derivative of Formula III).

FIGS. **7**A-**7**T show particularly suitable xanthone derivatives that can be formed (with "Me" representing a methyl group, as is commonly used in the art).

EXAMPLES

General One-Pot Experimental Procedure for Synthesis of Ortho-Acylation Products

Phenols/Thiophenol (1.3 equiv), aldehydes (1 equiv.), K_3PO_4 (2.2 equiv.), $CuCl_2$, $PdCl_2$ or $Pd(OAc)_2$ (5 mol %) and PPh_3 (7.5 mol %) were added in 3 mL toluene, and then the reaction stirred at 110° C. for 24 h. The mixture was extracted with DCM, washed by water, brine, and then the combined organic layer was dried by anhydrous Na_2SO_4. After evaporation of solvents, the crude product was purified by flash chromatography to afford ortho-acylation derivatives.

General One-Pot Experimental Procedure for Synthesis of Xanthone Derivatives

2-nitro/halides/alkoxy substituted-Phenols/Thiophenol (1.3 equiv), aldehydes (1 equiv.), K_3PO_4 (2.2 equiv.), $CuCl_2$, $PdCl_2$ or $Pd(OAc)_2$ (5 mol %) and PPh_3 (7.5 mol %) were added in 3 mL toluene, and then the reaction stirred at 110° C. for 24 h. The mixture was extracted with DCM, washed by water, brine, and then the combined organic layer was dried by anhydrous Na_2SO_4. After evaporation of solvents, the crude product was purified by flash chromatography to afford xanthone derivatives.

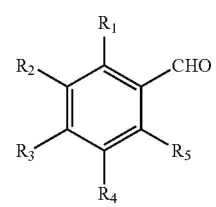
Xanthone derivatives having the general structures shown in FIGS. **7**A-**7**T were made according to the above described method. Each structure was confirmed by ^{1}HNMR, ^{13}C NMR, and MS data.

These and other modifications and variations to the present invention may be practiced by those of ordinary skill in the art, without departing from the spirit and scope of the present invention, which is more particularly set forth in the appended claims. In addition, it should be understood the aspects of the various embodiments may be interchanged both in whole or in part. Furthermore, those of ordinary skill in the art will appreciate that the foregoing description is by way of example only, and is not intended to limit the invention so further described in the appended claims.

The invention claimed is:

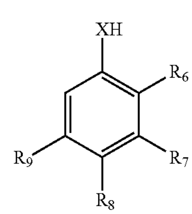
1. A method of forming a xanthone derivative, the method comprising: reacting a 2-substituted benzaldehyde with a phenol derivative in the presence of a catalyst system including a palladium catalyst and a copper catalyst to form the xanthone derivative;

wherein the 2-substituted benzaldehyde has a structure;

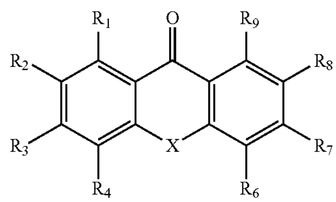


where R_1, R_2, R_3, and R_4 are, independently, H, an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group; and where R_5 is F, Cl, Br, I, a nitro group, or an alkoxy group; and

wherein the phenol derivative has a structure:



where R_5, R_7, R_3, and R_9 are, independently, H, an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group; a hydroxyl group, a nitro group, or a cyano group; and X is O, S, or NH, and wherein the xanthone derivative formed has a structure:



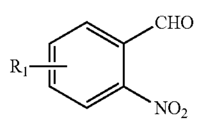
where R_1, R_2, R_3, R_4, R_6, R_7, R_8, R_9 are as defined above.

2. The method of claim **1**, wherein R_5 is a nitro group.

3. The method of claim **1**, wherein at least three of R_1, R_2, R_3, and R_4 are H.

4. The method of claim **3**, wherein only three of R_1, R_2, R_3 and R_4 are H and the only one that is not H is selected from an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group.

5. The method of claim **1**, wherein the 2-substituted benzaldehyde has a structure:



where R_1 is H, an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group.

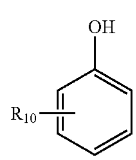
6. The method of claim **5**, wherein R_1 is an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group.

7. The method of claim **1**, wherein at least three of R_6, R_7, R_8, and R_9 are H.

8. The method of claim **7**, wherein only three of R_6, R_7, R_8 and R_9 are H and the only one that is not H is selected from an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group.

9. The method of claim **1**, wherein X is O.

10. The method of claim **1**, wherein the phenol derivative has a structure:

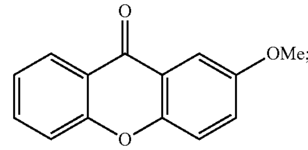


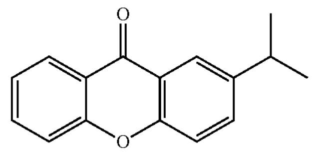
where R_{10} is H, an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group.

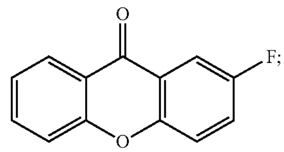
11. The method of claim **10**, wherein R_{10} is an aryl group, an alkyl group, an alkoxy group, a halide group, an amine group, a hydroxyl group, a nitro group, or a cyano group.

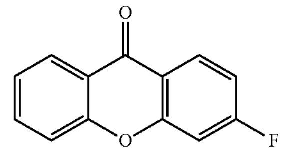
12. The method of claim **1**, wherein the 2-substituted benzaldehyde is reacted with the phenol derivative in the presence of triphenylphosphine.

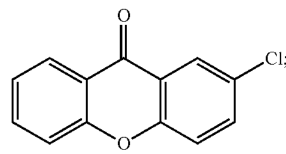
13. The method of claim **1**, wherein the xanthene derivative is selected from the group consisting of:

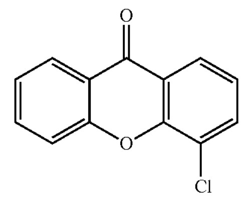


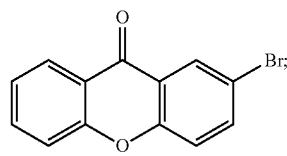


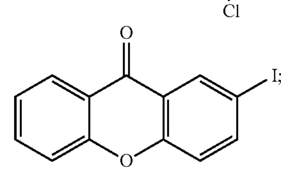


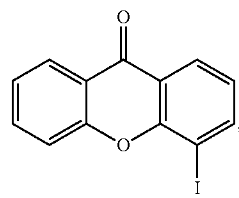


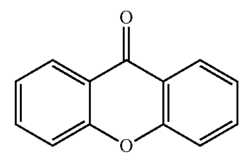


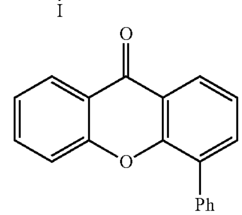


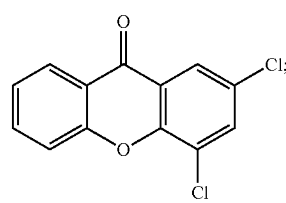


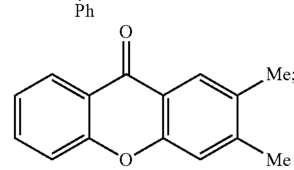


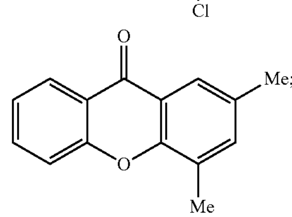


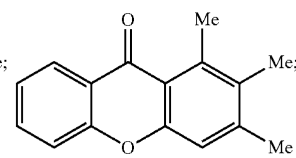


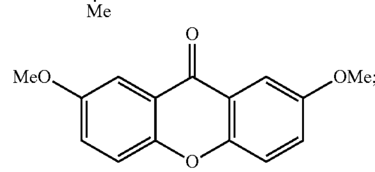












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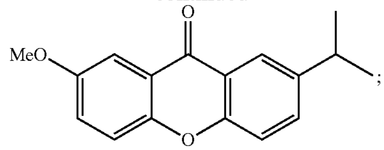

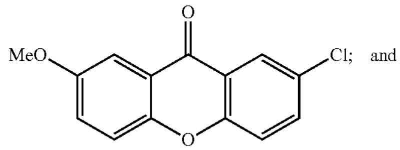

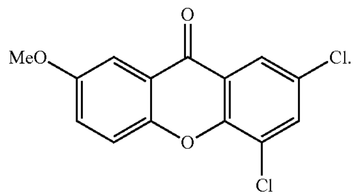

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